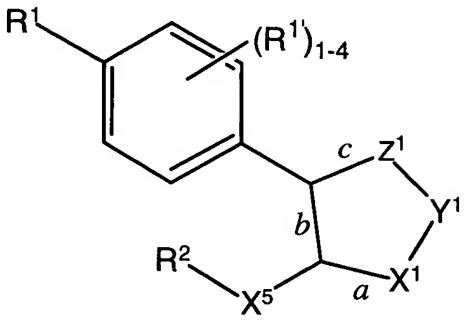
CLAIMS

What is claimed is:

1. A compound of Formula (I), (II), (III), (IV), (V), (VI), (VII) or (VIII), or a pharmaceutically acceptable salt thereof;

wherein the compound of Formula (I) is:



I

wherein:

when side *b* is a double bond, and sides *a* and *c* are single bonds, $-X^1-Y^1-Z^1-$ is:

(a) $-CR^4(R^5)-CR^5(R^{5'})-CR^4(R^5)-$;

(b) $-C(O)-CR^4(R^{4'})-CR^5(R^{5'})-$;

(c) $-CR^4(R^{4'})-CR^5(R^{5'})-C(O)-$;

(d) $-(CR^5(R^{5'}))_k-O-C(O)-$;

(e) $-C(O)-O-(CR^5(R^{5'}))_k-$;

(f) $-CR^4(R^{4'})-NR^3-CR^5(R^{5'})-$;

(g) $-CR^5(R^{5'})-NR^3-C(O)-$;

(h) $-CR^4=CR^{4'}-S-$;

(i) $-S-CR^4=CR^{4'}-$;

(j) $-S-N=CR^4-$;

(k) $-CR^4=N-S-$;

(l) $-N=CR^4-O-$;

(m) $-O-CR^4=N-$;

(n) $-NR^3-CR^4=N-$;

(o) $-N=CR^4-S-$;

(p) -S-CR^4=N-;

(q) -C(O)-NR^3-$CR^{5'}(R^{5'})$-;

(r) -R^3N-CR^5=C $R^{5'}$-;

(s) -CR^4=CR^5-NR^3-;

(t) -O-N=CR^4-;

(u) -CR^4=N-O-;

(v) -N=N-S-;

(w) -S-N=N-;

(x) -N=CR^4-NR^3-;

(y) -R^3N-N=N-;

(z) -N=N-NR^3-;

(aa) -$CR^4(R^{4'})$-O-$CR^5(R^{5'})$-;

(bb) -$CR^4(R^{4'})$-S-$CR^5(R^{5'})$-;

(cc) -$CR^4(R^{4'})$- C(O)-$CR^5(R^{5'})$-;

(dd) -$CR^4(R^{4'})$-$CR^5(R^{5'})$-C(S)-;

(ee) –$(CR^5(R^{5'}))_k$-O-C(S)-;

(ff) -C(S)-O-$(CR^5(R^{5'}))_k$-;

(gg) –$(CR^5(R^{5'}))_k$-NR^3-C(S)-;

(hh) -C(S)-NR^3-$(CR^5(R^{5'}))_k$-;

(ii) –$(CR^5(R^{5'}))_k$-S-C(O)-;

(jj) -C(O)-S-$(CR^5(R^{5'}))_k$-;

(kk) -O-CR^4=CR^5-;

(ll) -CR^4=CR^5-O-;

(mm) –C(O)- NR^3-S-;

(nn) -S-NR^3-C(O)-;

(oo) –C(O)-NR^3-O-;

(pp) –O-NR^3-C(O)-;

(qq) -NR^3-CR^4=CR^5-;

(rr) -CR^4=N-NR^3-;

(ss) -NR^3-N=CR^4-;

(tt) -C(O)-NR^3-NR^3-;

(uu) -NR^3-NR^3-C(O)-;

(vv) -C(O)-O-NR^3-;

(ww) -NR^3-O-C(O)-;

(xx) -O-$CR^4R^{4'}$-C(S)-;

(zz) -O-$CR^4R^{4'}$-C(O)-;

(aaa) -C(S)-$CR^4R^{4'}$-O-; or

(yy) -C(O)-$CR^4R^{4'}$-O-;

when sides *a* and *c* are double bonds and side *b* is a single bond, -X^1-Y^1-Z^1- is:

(a) =CR^4-O-CR^5=;

(b) =CR^4-NR^3-CR^5=;

(c) =N-S-CR^4=;

(d) =CR^4-S-N=;

(e) =N-O-CR^4=;

(f) =CR^4-O-N=;

(g) =N-S-N=;

(h) =N-O-N=;

(i) =N-NR^3-CR^4=;

(j) =CR^4-NR^3-N=;

(k) =N-NR^3-N=;

(l) =CR^4-S-CR^5=; or

(m) =CR^4-$CR^4(R^{4'})$-CR^5=;

R^1 is:

(a) -$S(O)_2$-CH_3;

(b) -$S(O)_2$-$NR^8(D^1)$;

(c) -$S(O)_2$-$N(D^1)$-C(O)-CF_3;

(d) -S(O)-(NH)-$NH(D^1)$;

(e) -S(O)-(NH)-$N(D^1)$-C(O)-CF_3;

(f) -$P(O)(CH_3)NH(D^1)$;

(g) -$P(O)(CH_3)_2$;

(h) -C(S)-$NH(D^1)$;

(i) -S(O)(NH)CH_3;

(j) -P(O)(CH_3)OD^1; or

(k) -P(O)(CH_3)NH(D^1);

$R^{1'}$ at each occurrence is independently:

(a) hydrogen;

(b) halogen;

(c) methyl; or

(d) CH_2OH;

R^2 is:

(a) lower alkyl;

(b) cycloalkyl;

(c) mono-, di- or tri-substituted phenyl or naphthyl, wherein the substituents are each independently:

(1) hydrogen;

(2) halo;

(3) alkoxy;

(4) alkylthio;

(5) CN;

(6) haloalkyl, preferably CF_3;

(7) lower alkyl;

(8) N_3;

(9) -CO_2D^1;

(10) -CO_2-lower alkyl;

(11) –($C(R^5)(R^6))_z$-OD^1;

(12) –($C(R^5)(R^6))_z$-O-lower alkyl;

(13) lower alkyl-CO_2-R^5 ;

(14) -OD^1;

(15) haloalkoxy;

(16) amino;

(17) nitro;

(18) alkylsulfinyl; or

(19) heteroaryl;

(d) mono-, di- or tri-substituted heteroaryl, wherein the heteroaryl is a monocyclic aromatic ring of 5 atoms, said ring having one heteroatom which is S, O, or N, and, optionally, 1, 2, or 3 additional N atoms; or the heteroaryl is a monocyclic ring of 6 atoms, said ring having one heteroatom which is N, and, optionally, 1, 2, 3, or 4 additional N atoms; wherein the substituents are each independently:

(1) hydrogen;

(2) halo;

(3) lower alkyl;

(4) alkoxy;

(5) alkylthio;

(6) CN;

(7) haloalkyl, preferably CF_3;

(8) N_3;

(9) $-C(R^5)(R^6)-OD^1$;

(10) $-C(R^5)(R^6)$-O-lower alkyl; or

(11) alkylsulfinyl;

(e) benzoheteroaryl which includes the benzo fused analogs of (d);

(f) $-NR^{10}R^{11}$;

(g) $-SR^{11}$;

(h) $-OR^{11}$;

(i) $-R^{11}$;

(j) alkenyl;

(k) alkynyl;

(l) unsubstituted, mono-, di-, tri- or tetra-substituted cycloalkenyl, wherein the substituents are each independently:

(1) halo;

(2) alkoxy;

(3) alkylthio;

(4) CN;

(5) haloalkyl, preferably CF_3;

(6) lower alkyl;

(7) N_3;

(8) $-CO_2D^1$;

(9) $-CO_2$-lower alkyl;

(10) $-C(R^{12})(R^{13})-OD^1$;

(11) $-C(R^{12})(R^{13})$-O-lower alkyl;

(12) lower alkyl-CO_2-R^{12} ;

(13) benzyloxy;

(14) -O-(lower alkyl)-CO_2R^{12};

(15) -O-(lower alkyl)-$NR^{12}\ R^{13}$; or

(16) alkylsulfinyl;

(m) mono-, di-, tri- or tetra-substituted heterocycloalkyl group of 5, 6 or 7 members, or a benzoheterocycle, wherein said heterocycloalkyl or benzoheterocycle contains 1 or 2 heteroatoms selected from O, S, or N and, optionally, contains a carbonyl group or a sulfonyl group, and wherein said substituents are each independently:

(1) halo;

(2) lower alkyl;

(3) alkoxy;

(4) alkylthio;

(5) CN;

(6) haloalkyl, preferably CF_3;

(7) N_3;

(8) $-C(R^{12})(R^{13})-OD^1$;

(9) $-C(R^{12})(R^{13})$-O-lower alkyl; or

(10) alkylsulfinyl;

(n) styryl, mono or di-substituted styryl, wherein the substituent are each independently:

(1) halo;

(2) alkoxy;

(3) alkylthio;

(4) CN;

(5) haloalkyl, preferably CF_3;

(6) lower alkyl;

(7) N_3;

(8) $-CO_2D^1$;

(9) $-CO_2$-lower alkyl;

(10) $-C(R^{12})(R^{13})-OD^1$;

(11) $-C(R^{12})(R^{13})$-O-lower alkyl;

(12) lower alkyl-CO_2-R^{12} ;

(13) benzyloxy;

(14) -O-(lower alkyl)-CO_2R^{12}; or

(15) -O-(lower alkyl)-$NR^{12}R^{13}$;

(o) phenylacetylene, mono- or di-substituted phenylacetylene, wherein the substituents are each independently:

(1) halo;

(2) alkoxy;

(3) alkylthio;

(4) CN;

(5) haloalkyl, preferably CF_3;

(6) lower alkyl;

(7) N_3;

(8) $-CO_2D^1$;

(9) $-CO_2$-lower alkyl;

(10) $-C(R^{12})(R^{13})-OD^1$;

(11) $-C(R^{12})(R^{13})$-O-lower alkyl;

(12) lower alkyl-CO_2-R^{12};

(13) benzyloxy;

(14) -O-(lower alkyl)-CO_2R^{12}; or

(15) -O-(lower alkyl)-$NR^{12}R^{13}$;

(p) fluoroalkenyl;

(q) mono- or di-substituted bicyclic heteroaryl of 8, 9 or 10 members, containing 2, 3, 4 or 5 heteroatoms, wherein at least one heteroatom resides on each ring of said bicyclic heteroaryl, said heteroatoms are each independently O, S and N and said substituents are each

independently:

(1) hydrogen;

(2) halo;

(3) lower alkyl;

(4) alkoxy;

(5) alkylthio;

(6) CN;

(7) haloalkyl, preferably CF_3;

(8) N_3;

(9) $-C(R^5)(R^6)-OD^1$; or

(10) $-C(R^5)(R^6)$-O-lower alkyl;

(r) K;

(s) aryl;

(t) arylalkyl;

(u) cycloalkylalkyl;

(v) $-C(O)R^{11}$;

(u) hydrogen;

(v) arylalkenyl;

(w) arylalkoxy;

(x) alkoxy;

(y) aryloxy;

(z) cycloalkoxy;

(aa) arylthio;

(bb) alkylthio;

(cc) arylalkylthio; or

(dd) cycloalkylthio;

R^3 is:

(a) hydrogen;

(b) haloalkyl, preferably CF_3;

(c) CN;

(d) lower alkyl;

(e) $-(C(R_e)(R_f))_p$-U-V;

(f) K;

(g) unsubstituted or substituted:

(1) lower alkyl-Q;

(2) lower alkyl-O- lower alkyl-Q;

(3) lower alkyl-S-lower alkyl-Q;

(4) lower alkyl-O-Q;

(5) lower alkyl-S-Q;

(6) lower alkyl-O-V;

(7) lower alkyl-S-V;

(8) lower alkyl-O-K; or

(9) lower alkyl-S-K;

wherein the substituent(s) reside on the lower alkyl group;

(h) Q;

(i) alkylcarbonyl;

(j) arylcarbonyl;

(k) alkylarylcarbonyl;

(l) arylalkylcarbonyl;

(m) carboxylic ester;

(n) carboxamido;

(o) cycloalkyl;

(p) mono-, di- or tri-substituted phenyl or naphthyl, wherein the substituents are each independently:

(1) hydrogen;

(2) halo;

(3) alkoxy;

(4) alkylthio;

(5) CN;

(6) haloalkyl, preferably CF_3;

(7) lower alkyl;

(8) N_3;

(9) -CO_2D^1;

(10) -CO_2-lower alkyl;

(11) –$(C(R^5)(R^6))_z$-OD^1;

(12) –$(C(R^5)(R^6))_z$-O-lower alkyl;

(13) lower alkyl-CO_2-R^5 ;

(14) -OD^1;

(15) haloalkoxy;

(16) amino;

(17) nitro; or

(18) alkylsulfinyl;

(q) alkenyl;

(r) alkynyl;

(s) arylalkyl;

(t) lower alkyl-OD^1;

(u) alkoxyalkyl;

(v) aminoalkyl;

(w) lower alkyl-CO_2R^{10};

(x) lower alkyl-$C(O)NR^{10}(R^{10'})$;

(y) heterocyclicalkyl; or

(z) heterocyclic ring-C(O)-;

R^4, $R^{4'}$, R^5 and $R^{5'}$ are each independently:

(a) hydrogen;

(b) amino;

(c) CN;

(d) lower alkyl;

(e) haloalkyl;

(f) alkoxy;

(g) alkylthio;

(h) Q;

(i) -O-Q;

(j) -S-Q;

(k) K;

(l) cycloalkoxy;

(m) cycloalkylthio;

(n) unsubstituted, mono-, or di-substituted phenyl or unsubstituted, mono-, or di-substituted benzyl, wherein the substituents are each independently:

(1) halo;

(2) lower alkyl;

(3) alkoxy;

(4) alkylthio;

(5) CN;

(6) haloalkyl, preferably CF_3;

(7) N_3;

(8) Q;

(9) nitro; or

(10) amino;

(o) unsubstituted, mono-, or di-substituted heteroaryl or unsubstituted, mono-, or di-substituted heteroarylmethyl, wherein the heteroaryl is a monocyclic aromatic ring of 5 atoms, said ring having one heteroatom which is S, O, or N, and, optionally, 1, 2, or 3 additional N atoms; or the heteroaryl is a monocyclic ring of 6 atoms, said ring having one heteroatom which is N, and, optionally, 1, 2, 3, or 4 additional N atoms; said substituents are each independently:

(1) halo;

(2) lower alkyl;

(3) alkoxy;

(4) alkylthio;

(5) CN;

(6) haloalkyl, preferably CF_3;

(7) N_3;

(8) $-C(R^6)(R^7)-OD^1$;

(9) $-C(R^6)(R^7)$-O-lower alkyl; or

(10) alkylsulfinyl

(p) $-CON(R^8)(R^8)$;

(q) -CH_2OR^8;

(r) -CH_2OCN;

(s) unsubstituted or substituted:

(1) lower alkyl-Q;

(2) -O-lower alkyl-Q;

(3) -S-lower alkyl-Q;

(4) lower alkyl-O-lower alkyl-Q;

(5) lower alkyl-S-lower alkyl-Q;

(6) lower alkyl-O-Q;

(7) lower alkyl-S-Q;

(8) lower alkyl-O-K;

(9) lower alkyl-S-K;

(10) lower alkyl-O-V; or

(11) lower alkyl-S-V;

wherein the substituent(s) resides on the lower alkyl;

(t) cycloalkyl;

(u) aryl;

(v) arylalkyl;

(w) cycloalkylalkyl;

(x) aryloxy;

(y) arylalkoxy;

(z) arylalkylthio;

(aa) cycloalkylalkoxy;

(bb) heterocycloalkyl;

(cc) alkylsulfonyloxy;

(dd) alkylsulfonyl;

(ee) arylsulfonyl;

(ff) arylsulfonyloxy;

(gg) -$C(O)R^{10}$;

(hh) nitro;

(ii) amino;

(jj) aminoalkyl;

(kk) -C(O)-alkyl-heterocyclic ring;

(ll) halo;

(mm) heterocyclic ring;

(nn) $-CO_2D^1$;

(oo) carboxyl;

(pp) amidyl; or

(qq) alkoxyalkyl;

alternatively, R^4 and R^5 together with the carbons to which they are attached are:

(a) cycloalkyl;

(b) aryl; or

(c) heterocyclic ring;

alternatively, R^4 and $R^{4'}$ or R^5 and $R^{5'}$ taken together with the carbon to which they are attached are:

(a) cycloalkyl; or

(b) heterocyclic ring;

alternatively, R^4 and R^5, $R^{4'}$ and $R^{5'}$, R^4 and $R^{5'}$, or $R^{4'}$ and R^5 when substituents on adjacent carbon atoms taken together with the carbons to which they are attached are:

(a) cycloalkyl;

(b) heterocyclic ring; or

(c) aryl;

R^6 and R^7 are each independently:

(a) hydrogen;

(b) unsubstituted, mono- or di-substituted phenyl; unsubstituted, mono- or di-substituted benzyl; unsubstituted, mono- or di-substituted heteroaryl; mono- or di-substituted heteroarylmethyl, wherein said substituents are each independently:

(1) halo;

(2) lower alkyl;

(3) alkoxy;

(4) alkylthio;

(5) CN;

(6) haloalkyl, preferably CF_3;

(7) N_3;

(8) $-C(R^{14})(R^{15})-OD^1$; or

(9) $-C(R^{14})(R^{15})$-O-lower alkyl;

(c) lower alkyl;

(d) $-CH_2OR^8$;

(e) CN;

(f) $-CH_2CN$;

(g) haloalkyl, preferably fluoroalkyl;

(h) $-CON(R^8)(R^8)$;

(i) halo; or

(j) $-OR^8$;

R^8 is:

(a) hydrogen;

(b) K; or

(c) R^9 ;

alternatively, R^5 and $R^{5'}$, R^6 and R^7 or R^7 and R^8 together with the carbon to which they are attached form a saturated monocyclic ring of 3, 4, 5, 6 or 7 atoms; optionally containing up to two heteroatoms selected from oxygen, $S(O)_o$ or NR_i;

R^9 is:

(a) lower alkyl;

(b) lower alkyl-CO_2D^1;

(c) lower alkyl-NHD^1;

(d) phenyl or mono-, di- or tri-substituted phenyl, wherein the substituents are each independently:

(1) halo;

(2) lower alkyl;

(3) alkoxy;

(4) alkylthio;

(5) lower alkyl-CO_2D^1;

(6) lower alkyl-NHD^1;

(7) CN;

(8) CO_2D^1; or

(9) haloalkyl, preferably fluoroalkyl;

(e) benzyl, mono-, di- or tri-substituted benzyl, wherein the substituents are each independently:

(1) halo;

(2) lower alkyl;

(3) alkoxy;

(4) alkylthio;

(5) lower alkyl-CO_2D^1;

(6) lower alkyl-NHD^1;

(7) CN;

(8) -CO_2D^1; or

(9) haloalkyl, preferably CF_3;

(f) cycloalkyl;

(g) K; or

(h) benzoyl, mono-, di-, or trisubstituted benzoyl, wherein the substituents are each independently:

(1) halo;

(2) lower alkyl;

(3) alkoxy;

(4) alkylthio;

(5) lower alkyl-CO_2D^1;

(6) lower alkyl-NHD^1;

(7) CN;

(8) -CO_2D^1; or

(9) haloalkyl, preferably CF_3;

R^{10} and $R^{10,}$ are each independently:

(a) hydrogen; or

(b) R^{11};

R^{11} is:

(a) lower alkyl;

(b) cycloalkyl;

(c) unsubstituted, mono-, di- or tri-substituted phenyl or naphthyl, wherein the substituents are each independently:

(1) halo;

(2) alkoxy;

(3) alkylthio;

(4) CN;

(5) haloalkyl, preferably CF_3;

(6) lower alkyl;

(7) N_3;

(8) $-CO_2D^1$;

(9) $-CO_2$-lower alkyl;

(10) $-C(R^{12})(R^{13})-OD^1$;

(11) $-C(R^{12})(R^{13})$-O-lower alkyl;

(12) lower alkyl-CO_2D^1;

(13) lower alkyl-CO_2R^{12};

(14) benzyloxy;

(15) -O-(lower alkyl)-CO_2D^1;

(16) -O-(lower alkyl)-CO_2R^{12}; or

(17) -O-(lower alkyl)-$NR^{12}R^{13}$;

(d) unsubstituted, mono-, di- or tri-substituted heteroaryl, wherein the heteroaryl is a monocyclic aromatic ring of 5 atoms, said ring having one heteroatom which is S, O, or N, and, optionally, 1, 2, or 3 additional N atoms; or said heteroaryl is a monocyclic ring of 6 atoms, said ring having one heteroatom which is N, and, optionally 1, 2, or 3 additional N atoms, and wherein said substituents are each independently:

(1) halo;

(2) lower alkyl;

(3) alkoxy;

(4) alkylthio;

(5) CN;

(6) haloalkyl, preferably CF_3;

(7) N_3;

(8) $-C(R^{12})(R^{13})-OD^1$; or

(9) $-C(R^{12})(R^{13})$-O-lower alkyl;

(e) unsubstituted, mono- or di-substituted benzoheterocycle, wherein the benzoheterocycle is a 5, 6, or 7-membered ring which contains 1 or 2 heteroatoms independently selected from O, S, or N, and, optionally, a carbonyl group or a sulfonyl group, wherein said substituents are each independently:

(1) halo;

(2) lower alkyl;

(3) alkoxy;

(4) alkylthio;

(5) CN;

(6) haloalkyl, preferably CF_3;

(7) N_3;

(8) $-C(R^{12})(R^{13})-OD^1$; or

(9) $-C(R^{12})(R^{13})$-O-lower alkyl;

(f) unsubstituted, mono- or di-substituted benzocarbocycle, wherein the carbocycle is a 5, 6, or 7-membered ring which optionally contains a carbonyl group, wherein said substituents are each independently :

(1) halo;

(2) lower alkyl;

(3) alkoxy;

(4) alkylthio;

(5) CN;

(6) haloalkyl, preferably CF_3;

(7) N_3;

(8) $-C(R^{12})(R^{13})-OD^1$; or

(9) $-C(R^{12})(R^{13})$-O-lower alkyl;

(g) hydrogen; or

(h) K

R^{12} and R^{13} are each independently:

(a) hydrogen;

(b) lower alkyl; or

(c) aryl; or

R^{12} and R^{13} together with the atom to which they are attached form a saturated monocyclic ring of 3, 4, 5, 6 or 7 atoms;

R^{14} and R^{15} are each independently :

(a) hydrogen; or

(b) lower alkyl; or

R^{14} and R^{15} together with the atom to which they are attached form a carbonyl, a thial, or a saturated monocyclic ring of 3, 4, 5, 6 or 7 atoms;

Q is:

(a) -C(O)-U-D^1;

(b) -CO_2-lower alkyl;

(c) tetrazolyl-5-yl;

(d) -C(R^7)(R^8)(S-D^1);

(e) -C(R^7)(R^8)(O-D^1); or

(f) -C(R^7)(R^8)(O-lower alkyl);

X^5 is:

(a) -($CR^{31}R^{32}$)$_a$-;

(b) -($CR^{31}R^{32}$)$_{bb}$-A^1-;

(c) -A^1-($CR^{31}R^{32}$)$_{bb}$-;

(d) –$CR^{31}R^{32}$-A^1-$CR^{31}R^{32}$-;

(e) –CR^{31}=; or

(f) -A^1;

A^1 is:

(a) oxygen;

(b) thio;

(c) sulfinyl;

(d) sulfonyl; or

(c) -N(R^{33})-;

R^{31} and R^{32} are each independently:

(a) hydrogen;

(b) lower alkyl;

(c) substituted lower alkyl;

(d) lower alkoxy;

(e) lower haloalkyl; or

(f) halo; or

R^{31} and R^{32} taken together are;

(a) oxo;

(b) thial;

(c) oxime; or

(d) hydrazone;

R^{33} is:

(a) lower alkyl;

(b) hydrogen; or

(c) -C(O)H;

a is an integer equal to 1 or 3;

bb is an integer equal to 2 or 3;

D^1 is:

(a) hydrogen or

(b) D;

D is:

(a) V; or

(b) K;

U is:

(a) oxygen;

(b) sulfur; or

(c) $-N(R_a)(R_i)-$;

V is:

(a) -NO;

(b) $-NO_2$; or

(c) hydrogen

K is $-W_{aa}-E_b-(C(R_e)(R_f))_p-E_c-(C(R_e)(R_f))_x-W_d-(C(R_e)(R_f))_y-W_i-E_j-W_g-(C(R_e)(R_f))_z-U-V$; wherein aa, b, c, d, g, i and j are each independently an integer from 0 to 3;

p, x, y and z are each independently an integer from 0 to 10;

W at each occurrence is independently:

(a) -C(O)-;

(b) -C(S)-;

(c) -T-;

(d) $-(C(R_e)(R_f))_h-$;

(e) alkyl;

(f) aryl;

(g) heterocyclic ring;

(h) arylheterocyclic ring, or

(i) $-(CH_2CH_2O)_q-$;

E at each occurrence is independently a -T- group, an alkyl group, an aryl group, a heterocyclic ring, $-(C(R_e)(R_f))_h-$, an arylheterocyclic ring or $-(CH_2CH_2O)_q-$;

h is an integer form 1 to 10;

q is an integer from 1 to 5;

R_e and R_f are each independently a hydrogen, an alkyl, a cycloalkoxy, a halogen, a hydroxy, an hydroxyalkyl, an alkoxyalkyl, an arylheterocyclic ring. a cycloalkylalkyl, a heterocyclicalkyl, an alkoxy, a haloalkoxy, an amino, an alkylamino, a dialkylamino, an arylamino, a diarylamino, an alkylarylamino, an alkoxyhaloalkyl, a haloalkoxy, a sulfonic acid, a sulfonic ester, an alkylsulfonic acid, an arylsulfonic acid, an arylalkoxy, an alkylthio, an arylthio, a cyano, an aminoalkyl, an aminoaryl, an aryl, an arylalkyl, a carboxamido, a alkylcarboxamido, an arylcarboxamido, an amidyl, a carboxyl, a carbamoyl, an alkylcarboxylic acid, an arylcarboxylic acid, an alkylcarbonyl, an arylcarbonyl, an ester, a carboxylic ester, an alkylcarboxylic ester, an arylcarboxylic ester, a haloalkoxy, a sulfonamido, an alkylsulfonamido, an arylsulfonamido, an alkylsulfonyl, an alkylsulfonyloxy, an arylsulfonyl, an arylsulfonyloxy, a urea, a nitro, -T-Q'-, or $-(C(R_g)(R_h))_k-T-Q'$ or R_e and R_f taken together are an oxo, a thial, a heterocyclic ring, a cycloalkyl group, an oxime, a hydrazone or a bridged cycloalkyl group;

Q' is -NO or $-NO_2$;

k is an integer from 1 to 3;

T is independently a covalent bond, a carbonyl, an oxygen, $-S(O)_o-$ or $-N(R_a)R_i-$,

o is an integer from 0 to 2,

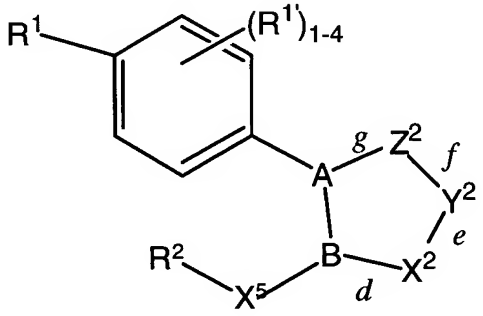
R_a is a lone pair of electrons, a hydrogen or an alkyl group;

R_i is a hydrogen, an alkyl, an aryl, an alkylcarboxylic acid, an arylcarboxylic acid, an alkylcarboxylic ester, an arylcarboxylic ester, an alkylcarboxamido, an arylcarboxamido, an alkylsulfinyl, an alkylsulfonyl, an alkylsulfonyloxy, an arylsulfinyl, an arylsulfonyloxy, an arylsulfonyl, a sulfonamido, a carboxamido, a carboxylic ester, an aminoalkyl, an aminoaryl, $-OR'_i$, $-CH_2-C(T-Q')(R_g)(R_h)$, a bond to an adjacent atom creating a double bond to that atom or $-(N_2O_2-)^{-}\bullet M^+$, wherein M^+ is an organic or inorganic cation; with the proviso that when R_i is $-CH_2-C(T-Q')(R_g)(R_h)$ or $-(N_2O_2-)\bullet M^+$; then "-T-Q'" can be a hydrogen, an alkyl group, an alkoxyalkyl group, an aminoalkyl group, a hydroxy group or an aryl group;

R_g and R_h at each occurrence are independently R_e;

R'_i is independently selected from R_i;

wherein the compound of Formula (II) is:



II

wherein:

A-B is:

(a) N-C;

(b) C-N; or

(c) N-N;

when A-B is N-C, sides *d* and *f* are double bonds, and sides *e* and *g* are single bonds,

$-X^2-Y^2-Z^2-$ is:

(a) $=CR^4-CR^{4'}=CR^5-$;

(b) $=N-CR^4=CR^{4'}-$;

(c) $=N-CR^4=N-$;

(d) $=CR^4-N=CR^{4'}-$;

(e) $=CR^4-N=N-$;

(f) $=N-N=CR^4-$;

(g) $=N-N=N-$; or

(h) $=CR^4-CR^5=N-$;

when A-B is C-N, sides *e* and *g* are double bonds, and sides *d* and *f* are single bonds, $-X^2-Y^2-Z^2-$ is:

(a) $-CR^4=N-N=$;

(b) $-N=N-CR^4=$;

(c) $-CR^4=N-CR^{4'}=$;

(d) $-N=CR^4-N=$;

(e) $-CR^4=CR^{4'}-N=$;

(f) $-N=CR^4-CR^5=$;

(g) $-CR^4=CR^5-CR^{5'}=$; or

(h) $-N=N-N=$;

when A-B is C-N, side *g* is a double bond, and sides *d*, *e* and *f* are single bonds, $-X^2-Y^2-Z^2-$ is:

(a) $-C(O)-O-CR^4=$;

(b) $-C(O)-NR^3-CR^4=$;

(c) $-C(O)-S-CR^4=$; or

(d) $-C(H)R^4-C(OH)R^5-N=$;

when A-B is N-C, sides *d* is a double bond, and sides *e*, *f* and *g* are single bonds, $-X^2-Y^2-Z^2-$ is:

(a) $=CR^4-O-C(O)-$;

(b) $=CR^4-NR^3-C(O)-$;

(c) $=CR^4-S-C(O)-$; or

(d) $=N-C(OH)R^4-C(H)R^5-$;

when sides *f* is a double bond, and sides *d*, *e* and *g* are single bonds,

$-X^2-Y^2-Z^2-$ is:

(a) $-CH(R^4)-CR^5=N-$; or

(b) $-C(O)-CR^4=CR^5-$;

when sides *e* is a double bond, and sides *d*, *f* and *g* are single bonds,

$-X^2-Y^2-Z^2-$ is:

(a) $-N=CR^4-CH(R^5)-$; or

(b) $-CR^4=CR^5-C(O)-$;

when sides *d*, *e*, *f* and *g* are single bonds,

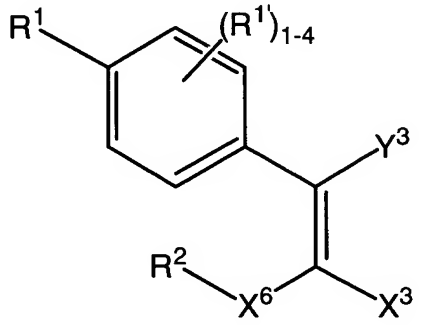
$-X^2-Y^2-Z^2-$ is:

(a) $-C(O)-CR^4(R^{4'})-C(O)-$; and

with the proviso that when A-B is C-N, then X^5 must be $-(CR^{31}R^{32})_a$ or $-(CR^{31}R^{32})_{bb}-A^1$; and

wherein R^1, $R^{1'}$, R^2, R^3, R^4, $R^{4'}$, R^5, $R^{5'}$, X^5 A^1, R^{31}, R^{32}, a and bb are as defined herein;

wherein the compound of Formula (III) is:



III

wherein:

X^3 is:

(a) $-C(O)-U-D^1$;

(b) $-CH_2-U-D^1$;

(c) $-CH_2-C(O)-CH_3$;

(d) $-CH_2-CH_2-C(O)-U-D^1$;

(e) -CH_2-O-D^1;

(f) -C(O)H or

(g) –C(O)-U-R^{12};

Y^3 is:

(a) -$(CR^5(R^{5'}))_k$-U-D^1;

(b) -CH_3;

(c) -$CH_2OC(O)R^6$; or

(d) -C(O)H;

R^{82}, $R^{82'}$, R^{83} and $R^{83'}$ are each independently:

(a) hydrogen;

(b) hydroxy;

(c) alkyl;

(d) alkoxy;

(e) lower alkyl-OD^1;

(f) alkylthio;

(g) CN;

(h) -$C(O)R^{84}$; or

(i) -$OC(O)R^{85}$;

R^{84} is:

(a) hydrogen;

(b) lower alkyl; or

(c) alkoxy;

R^{85} is:

(a) lower alkyl;

(b) alkoxy

(c) unsubstituted, mono-, di- or tri-substituted phenyl or pyridyl, wherein the substituents are each independently:

(1) halo;

(2) alkoxy;

(3) haloalkyl;

(4) CN;

(5) -C(O)R^{84};

(6) lower alkyl;

(7) -S(O)$_o$-lower alkyl; or

(8) -OD^1;

alternatively, R^{82} and R^{83} or $R^{82'}$ and $R^{83'}$ taken together are:

(a) oxo;

(b) thial;

(c) =C$R^{86}R^{87}$; or

(d) =NR^{88};

R^{86} and R^{87} are each independently:

(a) hydrogen;

(b) lower alkyl;

(c) lower alkyl-OD^1;

(d) CN; or

(e)-C(O)R^{84};

R^{88} is:

(a) OD^1;

(b) alkoxy;

(c) lower alkyl; or

(d) unsubstituted, mono-, di- or tri-substituted phenyl or pyridyl, wherein the substituents are each independently:

(1) halo;

(2) alkoxy;

(3) haloalkyl;

(4) CN;

(5) -C(O)R^{84};

(6) lower alkyl;

(7) -S(O)$_o$-lower alkyl; or

(8) -OD^1;

X^6 is:

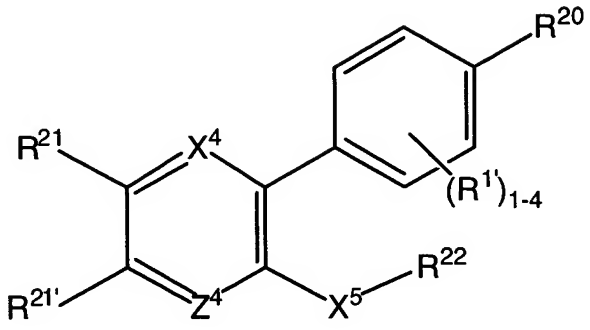
(a) -(C$R^{31}R^{32}$)$_a$-;

(b) -$(CR^{31}R^{32})_{bb}$-A^1-; or

(e) –CR^{31}=; and

wherein R^1, $R^{1'}$, R^2, R^5, $R^{5'}$, R^6, R^{12}, R^{31}, R^{32}, A^1, U, D^1, a, bb, o and k are as defined herein;

wherein the compound of Formula (IV) is:



IV

wherein:

X^4 and Z^4 are each independently:

(a) N; or

(b) CR^{21};

R^{20} is:

(a) -$S(O)_2$-CH_3;

(b) -$S(O)_2$-$NR^8(D^1)$; or

(c) -$S(O)_2$-$N(D^1)$-C(O)-CF_3;

R^{21} and $R^{21'}$ are each independently:

(a) hydrogen;

(b) lower alkyl;

(c) alkoxy;

(d) alkylthio;

(e) haloalkyl, preferably fluoroalkyl;

(f) haloalkoxy, preferably fluoroalkoxy;

(g) CN;

(h) -CO_2D^1;

(i) $-CO_2R^{14}$;

(j) lower alkyl-O-D^1;

(k) lower alkyl-CO_2D^1;

(l) lower alkyl-CO_2R^{14};

(m) halo;

(n) -O-D^1;

(o) $-N_3$;

(p) $-NO_2$;

(q) $-NR^{14}D^1$;

(r) $-N(D^1)C(O)R^{14}$;

(s) -NHK;

(t) aryl;

(u) arylalkylthio;

(v) arylalkoxy;

(w) alkylamino;

(x) aryloxy;

(y) alkylarylalkylamino;

(z) cycloalkylalkylamino; or

(aa) cycloalkylalkoxy;

R^{22} is:

(a) mono-, di- or tri-substituted phenyl or pyridinyl (or the N-oxide thereof), wherein the substituent are each independently:

(1) hydrogen;

(2) halo;

(3) alkoxy;

(4) alkylthio;

(5) CN;

(6) lower alkyl;

(7) haloalkyl, preferably fluoroalkyl;

(8) N_3;

(9) $-CO_2D^1$;

(10) -CO_2-lower alkyl;

(11) -$C(R^{14})(R^{15})$-OD^1;

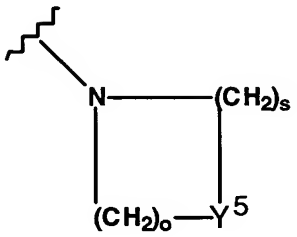
(12) -OD^1;

(13) lower alkyl-CO_2-R^{14}; or

(14) lower alkyl-CO_2-D^1;

(b) -T-$C(R^{23})(R^{24})$–$(C(R^{25})(R^{26}))_o$-$C(R^{27})(R^{28})$-U-D^1;

(c)



(d) arylalkyl; or

(e) cycloalkylalkyl;

wherein:

R^{14} and R^{15} are each independently:

(a) hydrogen; or

(b) lower alkyl;

R^{23}, R^{24}, R^{25}, R^{26}, R^{27}, R^{28} are each independently:

(a) hydrogen; or

(b) lower alkyl; or

R^{23} and R^{27}, or R^{27} and R^{28} together with the atoms to which they are attached form a carbocyclic ring of 3, 4, 5, 6 or 7 atoms, or R^{23} and R^{25} are joined to form a covalent bond;

Y^5 is:

(a) $CR^{29}R^{30}$;

(b) oxygen; or

(c) sulfur;

R^{29} and R^{30} are each independently:

(a) hydrogen;

(b) lower alkyl;

(c) $(CH_2)_o$-OD^1;

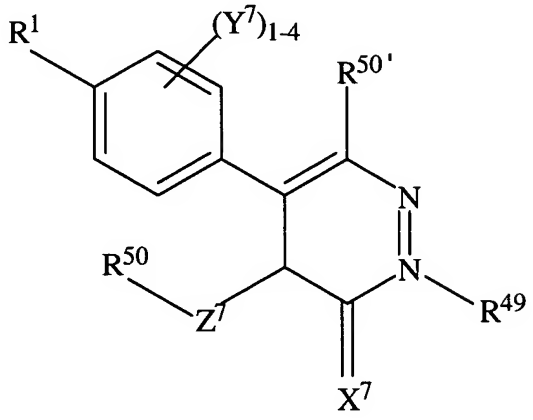
(d) halo; or

R^{29} and R^{30} taken together are an oxo group;

s is an integer from 2 to 4; and

wherein $R^{1'}$, R^8, X^5, D^1, T, U, K and o are as defined herein;

wherein the compound of Formula (V) is:



V

wherein:

X^7 is:

(a) oxygen;

(b) sulfur;

(c) $-NR^{51}$;

(d) -N-O-R^{52}; or

(e) -N-$NR^{52}R^{53}$;

Y^7 at each occurrence is independently:

(a) hydrogen;

(b) halo;

(c) lower alkyl;

(d) alkenyl; or

(e) alkynyl;

Z^7 is:

(a) $-(CR^{31}R^{32})_a$-;

R^{49} is:

(a) R^3; or

(b) R^4;

R^{50} and $R^{50'}$ are each independently:

(a) hydrogen;

(b) halo;

(c) lower alkyl;

(d) aryl;

(e) arylalkyl;

(f) cycloalkyl;

(g) cycloalkylalkyl;

(h) $-OD^1$;

(i) lower alkyl-OD^1;

(j) carboxamido;

(k) amidyl; or

(l) K;

R^{51} is:

(a) lower alkyl;

(b) alkenyl;

(c) cycloalkyl;

(d) cycloalkylalkyl;

(e) aryl;

(f) arylalkyl;

(g) heterocyclic ring; or

(h) lower alkyl-heterocyclic ring;

R^{52} and R^{53} are each independently:

(a) lower alkyl;

(b) cycloalkyl;

(c) cycloalkylalkyl;

(d) aryl;

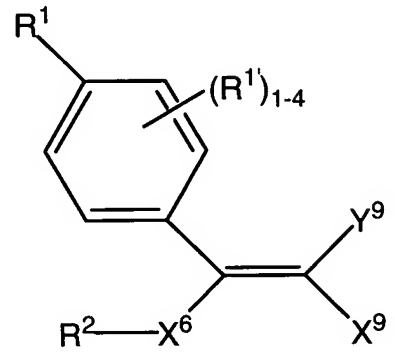
(e) arylalkyl;

(f) heterocyclic ring; or

(g) heterocyclicalkyl; and

wherein R^1, R^3, R^4, R^{31}, R^{32}, K, D^1 and a are as defined herein;

wherein the compound of Formula (VI) is:



VI

wherein:

X^9 is $-C(O)-U-D^1$ and Y^9 is $-CH_2-CR^5(R^{5'})-U-D^1$; or

X^9 is $-CH_2-CR^5(R^{5'})-U-D^1$ and Y^9 is $-C(O)-U-D^1$; or

X^9 and Y^9 taken together are:

(a) $-C(O)-O-CR^4(R^{4'})-CR^5(R^{5'})-$;

(b) $-(CR^4(R^{4'}))_k-CR^5(R^{5'})-CR^5(R^{5'})-$;

(c) $-C(O)-(CR^4(R^{4'}))_k-CR^5(R^{5'})-$;

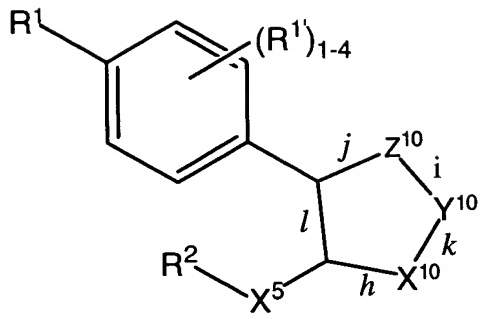
(d) $-(CR^4(R^{4'}))_k-CR^5(R^{5'})-C(O)-$; or

(e) $-C(O)-CR^4(R^{4'})-CR^5(R^{5'})-$;

wherein X^9 is the first carbon atom of a, b, c, d and e; and

wherein R^1, $R^{1'}$, R^2, R^4, $R^{4'}$, R^5, $R^{5'}$, X^6, U, D^1 and k are as defined herein;

wherein the compound of Formula (VII) is:

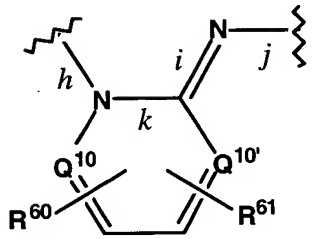


VII

wherein:

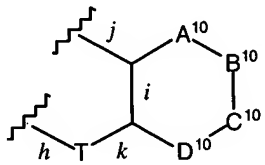
when side *h*, *k*, and *j* are single bonds, and side *i* and *l* are a double bond, -X^{10}-Y^{10}-Z^{10}- is:

(a)

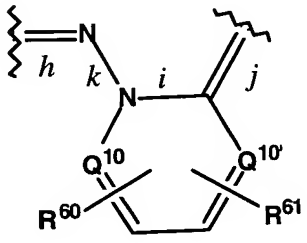


or

(b)

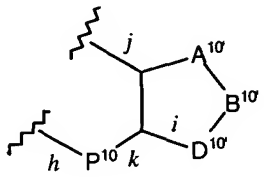


when sides *i* , *k* and *l* are single bonds, and sides *h* and *j* are double bonds, -X^{10}-Y^{10}-Z^{10}- is:



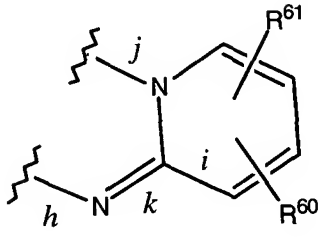
when side *h* and *j* are single bonds, *l* is a double bond, and side *k* and *i* is a single or a double bond, $-X^{10}-Y^{10}-Z^{10}-$ is:

(a)



or

(b)



P^{10} is:

(a) -N=;

(b) $-NR^3-$;

(c) -O-; or

(d) -S-;

Q^{10} and $Q^{10'}$ are each independently:

(a) CR^{60}; or

(b) nitrogen;

$A^{10}-B^{10}-C^{10}-D^{10}-$ is:

(a) $-CR^4=CR^{4'}-CR^5=CR^{5'}-$;

(b) $-CR^4(R^{4'})-CR^5(R^{5'})-CR^4(R^{4'})-C(O)-$;

(c) $-CR^4(R^{4'})-CR^5(R^{5'})-C(O)-CR^4(R^{4'})-$;

(d) $-CR^4(R^{4'})-C(O)-CR^4(R^{4'})-CR^5(R^{5'})-$;

(e) $-C(O)-CR^4(R^{4'})-CR^5(R^{5'})-CR^4(R^{4'})-$;

(f) -$CR^4(R^{4'})$-$CR^5(R^{5'})$-C(O)-;

(g) -$CR^4(R^{4'})$-C(O)-$CR^5(R^{5'})$-;

(h) -C(O)-$CR^4(R^{4'})$-$CR^5(R^{5'})$ -;

(i) -$CR^4(R^{4'})$-$CR^5(R^{5'})$-O-C(O)-;

(j) -$CR^4(R^{4'})$-O-C(O)-$CR^5(R^{5'})$ -;

(k) -O-C(O)-$CR^4(R^{4'})$-$CR^5(R^{5'})$ -;

(l) -$CR^4(R^{4'})$-$CR^5(R^{5'})$-C(O)-O-;

(m) -$CR^4(R^{4'})$-C(O)-O-$CR^5(R^{5'})$-;

(n) -C(O)-O-$CR^4(R^{4'})$-$CR^5(R^{5'})$-;

(o) -$CR^{12}(R^{13})$-O-C(O)-;

(p) -C(O)-O-$CR^{12}(R^{13})$-;

(q) -O-C(O)-$CR^{12}(R^{13})$-;

(r) -$CR^{12}(R^{13})$-C(O)-O-;

(s) -N=CR^4-$CR^{4'}$=CR^5-;

(t) -CR^4=N-$CR^{4'}$=CR^5-;

(u) -CR^4=$CR^{4'}$-N=CR^5-;

(v) -CR^4=CR^5-$CR^{5'}$=N-;

(w) -N=CR^4-$CR^{4'}$=N-;

(x) -N=CR^4-N=$CR^{4'}$-;

(y) -CR^4=N-$CR^{4'}$=N-;

(z) -S-CR^4=N-;

(aa) -S-N=CR^4-;

(bb) -N=N-NR^3-

(cc) -CR^4=N-S-;

(dd) -N=CR^4-S-;

(ee) -O-CR^4=N-;

(ff) -O-N=CR^4-; or

(gg) -N=CR^4-O-;

$A^{10,}$-$B^{10,}$-$D^{10,}$ is:

(a) -CR^4=CR^5-$CR^{5'}$=

(b) -$CR^4(R^{4'})$-$CR^5(R^{5'})$-$CR^4(R^{4'})$-;

(c) -C(O)-$CR^4(R^{4'})$-$CR^5(R^{5'})$-;

(d) -$CR^4(R^{4'})$-$CR^5(R^{5'})$-C(O)-;

(e) -N=CR^4-CR^5=;

(g) -N=N-CR^4=;

(h) -N=N-NR^3-;

(i) -N=N-N=;

(j) -N=CR^4-NR^3-;

(k) -N=CR^4-N=;

(l) -CR^4=N-NR^3-;

(m) -CR^4=N-N=;

(n) -CR^4=N-CR^5=;

(o) -CR^4=CR^5-NR^3-;

(p) -CR^4=CR^5-N=;

(q) -S-CR^4=CR^5-;

(r) -O-CR^4=CR^5;

(s) -CR^4=CR^5-O-;

(t) -CR^4=CR^5-S-;

(u) -CR^4=N-S-;

(v) -CR^4=N-O-;

(w) -N=CR^4-S-;

(x) -N=CR^4-O-;

(y) -S-CR^4=N-;

(z) -O-CR^4=N-;

(aa) -N=N-S-;

(bb) -N=N-O-;

(cc) -S-N=N-;

(dd) -O-N=N-;

(ee) -CR^4=CR^5-S;

(ff) -$CR^4(R^{4'})$-$CR^5(R^{5'})$-S-;

(gg) -$CR^4(R^{4'})$-$CR^5(R^{5'})$-O-;

(hh) -S-$CR^4(R^{4'})$-$CR^5(R^{5'})$-; or

(ii) -O-$CR^4(R^{4'})$-$CR^5(R^{5'})$-;

R^{60} and R^{61} are each independently:

(a) lower alkyl;

(b) haloalkyl, preferably fluoroalkyl;

(c) alkoxy;

(d) alkylthio;

(e) lower alkyl-OD^1;

(f) -C(O)H;

(h) -$(CH_2)_q$-CO_2-lower alkyl;

(i) -$(CH_2)_q$-CO_2D^1;

(j) -O-$(CH_2)_q$-S-lower alkyl;

(k) -$(CH_2)_q$-S-lower alkyl;

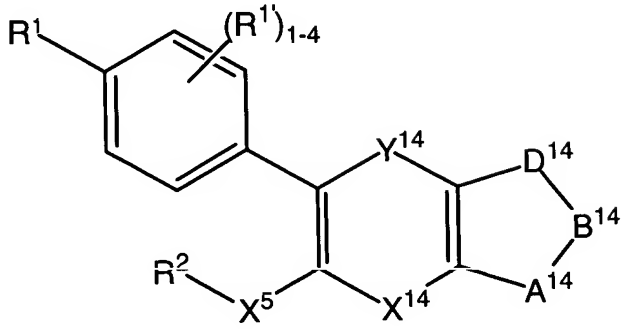
(l) -$S(O)_2$-lower alkyl;

(m) -$(CH_2)_q$-$NR^{12}R^{13}$; or

(n) -C(O)N(R^8)(R^8); and

wherein R^1, $R^{1'}$, R^2, R^3, R^4, $R^{4'}$, R^5, $R^{5'}$, R^8, R^{12}, R^{13}, X^5, T, D^1 and q are as defined herein;

wherein the compound of Formula (VIII) is:



VIII

wherein:

X^{14} is:

(a) -C(O)-; or

(b) -C(S)-;

Y^{14} is:

(a) -O-; or

(b) -S-;

A^{14}-B^{14}-D^{14}- is:

(a) $-CR^4=CR^{4'}-CR^5=CR^{5'}-$;

(b) $-CR^4(R^{4'})-CR^5(R^{5'})-C(O)-$;

(c) $-CR^4(R^{4'})-C(O)-CR^5(R^{5'})-$;

(d) $-C(O)-CR^4(R^{4'})-CR^5(R^{5'})$ -;

(e) $-CR^4(R^5)-O-C(O)-$;

(f) $-C(O)-O-CR^4(R^5)--$;

(g) $-O-C(O)-CR^4(R^5)-$;

(h) $-S-N=CR^4-$;

(i) $-O-N=CR^4-$;

(j) $-CR^4(R^5)-NR^3-C(O)-$;

(k) $-C(O)-NR^3-CR^4(R^5)--$;

(l) $-NR^3-C(O)-CR^4(R^5)-$;

(m) $-CR^4(R^5)-S-C(O)-$;

(n) $-C(O)-S-CR^4(R^5)--$;

(o) $-S-C(O)-CR^4(R^5)-$;

(p) $-CR^4=CR^{4'}-C(O)-$;

(q) $-C(O)-CR^4=CR^{4'}-$;

(r) $-O-CR^4=CR^{4'}-$;

(s) $-S-CR^4=CR^{4'}-$;

(t) $-NR^3-CR^4=CR^5-$;

(u) $-S-NR^3-C(O)-$;

(v) $-O-NR^3-C(O)-$; or

(w) $-NR^3-N=CR^4-$; and

wherein R^1, $R^{1'}$, R^2, R^3, R^4, $R^{4'}$, R^5, $R^{5'}$ and X^5 are as defined herein.

2. A composition comprising the compound of claim 1 and a pharmaceutically acceptable carrier.

3. A method for treating or reducing inflammation, pain or fever in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 2.

4. A method for treating a gastrointestinal disorder, or improving the gastrointestinal properties of a COX-2 inhibitor in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 2.

5. The method of claim 4, wherein the gastrointestinal disorder is an inflammatory bowel disease, Crohn's disease, gastritis, irritable bowel syndrome, ulcerative colitis, a peptic ulcer, a stress ulcer, a bleeding ulcer, gastric hyperacidity, dyspepsia, gastroparesis, Zollinger-Ellison syndrome, gastroesophageal reflux disease, a bacterial infection, short-bowel (anastomosis) syndrome, or a hypersecretory state associated with systemic mastocytosis or basophilic leukemia and hyperhistaminemia

6. A method for facilitating wound healing in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 2.

7. The method of claim 6, wherein the wound is an ulcer.

8. A method for treating or reversing renal and/or respiratory toxicity in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 2.

9. A method for treating a disorder resulting from elevated levels of COX-2 in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 2.

10. The method of claim 9, wherein the disorder resulting from elevated levels of COX-2 is angiogenesis, arthritis, asthma, bronchitis, menstrual cramps, premature labor, tendinitis, bursitis, a skin-related condition, neoplasia, an inflammatory process in a disease, an ophthalmic disorder, pulmonary inflammation, a central nervous system disorder, allergic rhinitis, respiratory distress syndrome, endotoxin shock syndrome, atherosclerosis, a microbial infection, a cardiovascular disorder, a urinary disorder, a urological disorder, endothelial dysfunction, organ deterioration, tissue deterioration, or activation, adhesion and infiltration of neutrophils at the site of inflammation.

11. The method of claim 10, wherein the neoplasia is a brain cancer, a bone cancer, an epithelial cell-derived neoplasia (epithelial carcinoma), a basal cell carcinoma, an adenocarcinoma, a gastrointestinal cancer, a lip cancer, a mouth cancer, an esophageal cancer, a small bowel cancer, a stomach cancer, a colon cancer, a liver cancer, a bladder cancer, a pancreas cancer, an ovary cancer, a cervical cancer, a lung cancer, a breast cancer, a skin cancer, a squamus cell cancer, a basal cell cancer, a prostate cancer, a renal cell carcinoma, a cancerous tumor, a growth, a polyp, an adenomatous polyp, a familial adenomatous polyposis or a fibrosis resulting from radiation therapy.

12. The method of claim 10, wherein the central nervous system disorder is cortical dementia, Alzheimer's disease, vascular dementia, multi-infarct dementia, pre-senile dementia, alcoholic dementia, senile dementia, or central nervous system damage resulting from stroke, ischemia or trauma.

13. A method for inhibiting platelet aggregation in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 2.

14. The composition of claim 2, further comprising at least one therapeutic agent.

15. The composition of claim 14, wherein the therapeutic agent is a steroid, a nonsteroidal antiinflammatory compound, a 5-lipoxygenase (5-LO) inhibitor, a leukotriene B_4 receptor antagonist, a leukotriene A_4 hydrolase inhibitor, a 5-HT agonist, a 3-hydroxy-3-methylglutaryl coenzyme A inhibitor, a H_2 antagonist, an antineoplastic agent, an antiplatelet agent, a thrombin inhibitor, a thromboxane inhibitor, a decongestant, a diuretic, a sedating or non-sedating anti-histamine, an inducible nitric oxide synthase inhibitor, an opioid, an analgesic, a *Helicobacter pylori* inhibitor, a proton pump inhibitor, an isoprostane inhibitor, or a mixture of two or more thereof.

16. The composition of claim 15, wherein the nonsteroidal antiinflammatory compound is acetaminophen, aspirin, diclofenac, ibuprofen, ketoprofen, indomethacin or naproxen.

17. A method for treating or reducing inflammation, pain or fever in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 14.

18. A method for treating a gastrointestinal disorder, or improving the gastrointestinal

properties of a COX-2 inhibitor in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 14.

19. The method of claim 18, wherein the gastrointestinal disorder is an inflammatory bowel disease, Crohn's disease, gastritis, irritable bowel syndrome, ulcerative colitis, a peptic ulcer, a stress ulcer, a bleeding ulcer, gastric hyperacidity, dyspepsia, gastroparesis, Zollinger-Ellison syndrome, gastroesophageal reflux disease, a bacterial infection, short-bowel (anastomosis) syndrome, or a hypersecretory state associated with systemic mastocytosis or basophilic leukemia and hyperhistaminemia.

20. A method for facilitating wound healing in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 14.

21. The method of claim 20, wherein the wound is an ulcer.

22. A method for treating or reversing renal and/or respiratory toxicity in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 14.

23. A method for treating a disorder resulting from elevated levels of COX-2 in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 14.

24. The method of claim 23, wherein the disorder resulting from elevated levels of COX-2 is angiogenesis, arthritis, asthma, bronchitis, menstrual cramps, premature labor, tendinitis, bursitis, a skin-related condition, neoplasia, an inflammatory process in a disease, an ophthalmic disorder, pulmonary inflammation, a central nervous system disorder, allergic rhinitis, respiratory distress syndrome, endotoxin shock syndrome, atherosclerosis, a microbial infection, a cardiovascular disorder, a urinary disorder, a urological disorder, endothelial dysfunction, organ deterioration, tissue deterioration, or activation, adhesion and infiltration of neutrophils at the site of inflammation.

25. The method of claim 24, wherein the neoplasia is a brain cancer, a bone cancer, an epithelial cell-derived neoplasia (epithelial carcinoma), a basal cell carcinoma, an adenocarcinoma, a gastrointestinal cancer, a lip cancer, a mouth cancer, an esophageal cancer, a small bowel cancer, a stomach cancer, a colon cancer, a liver cancer, a bladder cancer, a pancreas cancer, an ovary cancer, a cervical cancer, a lung cancer, a breast cancer, a skin cancer, a squamus cell cancer, a basal cell cancer, a prostate cancer, a renal cell carcinoma, a cancerous

tumor, a growth, a polyp, an adenomatous polyp, a familial adenomatous polyposis or a fibrosis resulting from radiation therapy.

26. The method of claim 24, wherein the central nervous system disorder is cortical dementia, Alzheimer's disease, vascular dementia, multi-infarct dementia, pre-senile dementia, alcoholic dementia, senile dementia, or central nervous system damage resulting from stroke, ischemia or trauma.

27. A method for inhibiting platelet aggregation in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 14.

28. A composition comprising at least one compound of claim 1 and at least one compound that donates, transfers or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase.

29. The composition of claim 28, further comprising a pharmaceutically acceptable carrier.

30. The composition of claim 28, wherein the compound that donates, transfers, or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor or is a substrate for nitric oxide synthase is an S-nitrosothiol.

31. The composition of claim 30, wherein the S-nitrosothiol is S-nitroso-N-acetylcysteine, S-nitroso-captopril, S-nitroso-N-acetylpenicillamine, S-nitroso-homocysteine, S-nitroso-cysteine, S-nitroso-glutathione, or S-nitroso-cysteinyl-glycine.

32. The composition of claim 30, wherein the S-nitrosothiol is:

(i) $HS(C(R_e)(R_f))_mSNO$;

(ii) $ONS(C(R_e)(R_f))_mR_e$; or

(iii) $H_2N\text{-}CH(CO_2H)\text{-}(CH_2)_m\text{-}C(O)NH\text{-}CH(CH_2SNO)\text{-}C(O)NH\text{-}CH_2\text{-}CO_2H$;

wherein m is an integer from 2 to 20; R_e and R_f are each independently a hydrogen, an alkyl, a cycloalkoxy, a halogen, a hydroxy, an hydroxyalkyl, an alkoxyalkyl, an arylheterocyclic ring. a cycloalkylalkyl, a heterocyclicalkyl, an alkoxy, a haloalkoxy, an amino, an alkylamino, a dialkylamino, an arylamino, a diarylamino, an alkylarylamino, an alkoxyhaloalkyl, a haloalkoxy, a sulfonic acid, a sulfonic ester, an alkylsulfonic acid, an arylsulfonic acid, an arylalkoxy, an alkylthio, an arylthio, a cyano, an aminoalkyl, an aminoaryl, an aryl, an arylalkyl, a

carboxamido, a alkylcarboxamido, an arylcarboxamido, an amidyl, a carboxyl, a carbamoyl, an alkylcarboxylic acid, an arylcarboxylic acid, an alkylcarbonyl, an arylcarbonyl, an ester, a carboxylic ester, an alkylcarboxylic ester, an arylcarboxylic ester, a haloalkoxy, a sulfonamido, an alkylsulfonamido, an arylsulfonamido, an alkylsulfonyl, an alkylsulfonyloxy, an arylsulfonyl, an arylsulfonyloxy, a urea, a nitro, -T-Q'-, or $-(C(R_g)(R_h))_k$-T-Q' or R_e and R_f taken together are an oxo, a methanthial, a heterocyclic ring, a cycloalkyl group, an oxime, a hydrazone or a bridged cycloalkyl group; Q' is -NO or $-NO_2$; and T is independently a covalent bond, a carbonyl, an oxygen, $-S(O)_o-$ or $-N(R_a)R_i-$, wherein o is an integer from 0 to 2, R_a is a lone pair of electrons, a hydrogen or an alkyl group; R_i is a hydrogen, an alkyl, an aryl, an alkylcarboxylic acid, an arylcarboxylic acid, an alkylcarboxylic ester, an arylcarboxylic ester, an alkylcarboxamido, an arylcarboxamido, an alkylsulfinyl, an alkylsulfonyl, an alkylsulfonyloxy, an arylsulfinyl, an arylsulfonyloxy, an arylsulfonyl, a sulfonamido, a carboxamido, a carboxylic ester, an aminoalkyl, an aminoaryl, $-CH_2-C(T-Q')(R_g)(R_h)$, or $-(N_2O_2-)^-\bullet M^+$, wherein M^+ is an organic or inorganic cation; with the proviso that when R_i is $-CH_2-C(T-Q')(R_g)(R_h)$ or $-(N_2O_2-)\bullet M^+$; then "-T-Q'" can be a hydrogen, an alkyl group, an alkoxyalkyl group, an aminoalkyl group, a hydroxy group or an aryl group; and R_g and R_h at each occurrence are independently R_e.

33. The composition of claim 28, wherein the compound that donates, transfers, or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase is L-arginine, L-homoarginine, N-hydroxy-L-arginine, nitrosated L-arginine, nitrosylated L-arginine, nitrosated N-hydroxy-L-arginine, nitrosylated N-hydroxy-L-arginine, nitrosated L-homoarginine, nitrosylated L-homoarginine), citrulline, ornithine, glutamine, lysine, an arginase inhibitor or a nitric oxide mediator.

34. The composition of claim 28, wherein the compound that donates, transfers, or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase is:

(i) a compound that comprises at least one ON-O- or ON-N- group;

(ii) a compound that comprises at least one O_2N-O-, O_2N-N- or O_2N-S- or group;

(iii) a N-oxo-N-nitrosoamine having the formula: $R^{1''}R^{2''}N$-N(O-M^+)-NO, wherein

$R^{1''}$ and $R^{2''}$ are each independently a polypeptide, an amino acid, a sugar, an oligonucleotide, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted hydrocarbon, or a heterocyclic group, and M^+ is an organic or inorganic cation.

35. The composition of claim 34, wherein the compound comprising at least one ON-O- or ON-N- group is an ON-O-polypeptide, an ON-N-polypeptide, an ON-O-amino acid, an ON-N-amino acid, an ON-O-sugar, an ON-N-sugar, an ON-O-oligonucleotide, an ON-N-oligonucleotide, a straight or branched, saturated or unsaturated, substituted or unsubstituted, aliphatic or aromatic ON-O-hydrocarbon, a straight or branched, saturated or unsaturated, substituted or unsubstituted, aliphatic or aromatic ON-N-hydrocarbon, an ON-O-heterocyclic compound or an ON-N-heterocyclic compound.

36. The composition of claim 34, wherein compound comprising at least one O_2N-O-, O_2N-N- or O_2N-S- group is an O_2N-O-polypeptide, an O_2N-N-polypeptide, an O_2N-S-polypeptide, an O_2N-O-amino acid, O_2N-N-amino acid, O_2N-S-amino acid, an O_2N-O-sugar, an O_2N-N-sugar, O_2N-S-sugar, an O_2N-O-oligonucleotide, an O_2N-N-oligonucleotide, an O_2N-S-oligonucleotide, , a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted O_2N-O-hydrocarbon, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted O_2N-N-hydrocarbon, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted O_2N-S-hydrocarbon, an O_2N-O-heterocyclic compound, an O_2N-N-heterocyclic compound or an O_2N-S-heterocyclic compound.

37. The composition of claim 28, further comprising at least one therapeutic agent.

38. The composition of claim 37, wherein the therapeutic agent is a steroid, a nonsteroidal antiinflammatory compound, a 5-lipoxygenase (5-LO) inhibitor, a leukotriene B_4 receptor antagonist, a leukotriene A_4 hydrolase inhibitor, a 5-HT agonist, a HMG CoA inhibitor, a H_2 antagonist, an antineoplastic agent, an antiplatelet agent, a thrombin inhibitor, a thromboxane inhibitor, a decongestant, a diuretic, a sedating or non-sedating anti-histamine, an inducible nitric oxide synthase inhibitor, an opioid, an analgesic, a *Helicobacter pylori* inhibitor, a proton pump inhibitor, an isoprostane inhibitor, or a mixture of two or more thereof.

39. The composition of claim 38, wherein the nonsteroidal antiinflammatory compound is acetaminophen, aspirin, diclofenac, ibuprofen, ketoprofen, indomethacin or naproxen.

40. A method for treating or reducing inflammation, pain or fever in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 29 or 37.

41. A method for treating a gastrointestinal disorder, or improving the gastrointestinal properties of a COX-2 inhibitor in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 29 or 37.

42 The method of claim 41, wherein the gastrointestinal disorder is an inflammatory bowel disease, Crohn's disease, gastritis, irritable bowel syndrome, ulcerative colitis, a peptic ulcer, a stress ulcer, a bleeding ulcer, gastric hyperacidity, dyspepsia, gastroparesis, Zollinger-Ellison syndrome, gastroesophageal reflux disease, a bacterial infection, short-bowel (anastomosis) syndrome, or a hypersecretory state associated with systemic mastocytosis or basophilic leukemia and hyperhistaminemia.

43. A method for facilitating wound healing in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 29 or 37.

44. The method of claim 43, wherein the wound is an ulcer.

45. A method for treating or reversing renal and/or respiratory toxicity in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 29 or 37.

46. A method for treating a disorder resulting from elevated levels of COX-2 in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 29 or 37.

47. The method of claim 46, wherein the disorder resulting from elevated levels of COX-2 is angiogenesis, arthritis, asthma, bronchitis, menstrual cramps, premature labor, tendinitis, bursitis, a skin-related condition, neoplasia, an inflammatory process in a disease, an ophthalmic disorder, pulmonary inflammation, a central nervous system disorder, allergic rhinitis, respiratory distress syndrome, endotoxin shock syndrome, atherosclerosis, a microbial infection, a cardiovascular disorder, a urinary disorder, a urological disorder, endothelial dysfunction, organ deterioration, tissue deterioration, or activation, adhesion and infiltration of neutrophils at the site of inflammation.

48. The method of claim 47, wherein the neoplasia is a brain cancer, a bone cancer,

an epithelial cell-derived neoplasia (epithelial carcinoma), a basal cell carcinoma, an adenocarcinoma, a gastrointestinal cancer, a lip cancer, a mouth cancer, an esophageal cancer, a small bowel cancer, a stomach cancer, a colon cancer, a liver cancer, a bladder cancer, a pancreas cancer, an ovary cancer, a cervical cancer, a lung cancer, a breast cancer, a skin cancer, a squamus cell cancer, a basal cell cancer, a prostate cancer, a renal cell carcinoma, a cancerous tumor, a growth, a polyp, an adenomatous polyp, a familial adenomatous polyposis or a fibrosis resulting from radiation therapy.

49. The method of claim 47, wherein the central nervous system disorder is cortical dementia, Alzheimer's disease, vascular dementia, multi-infarct dementia, pre-senile dementia, alcoholic dementia, senile dementia, or central nervous system damage resulting from stroke, ischemia or trauma.

50. A method for inhibiting platelet aggregation in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 29 or 37.

51. A kit comprising at least one compound of claim 1.

52. The kit of claim 51, further comprising (i) at least one compound that donates, transfers or releases nitric oxide, induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase; (ii) at least one therapeutic agent; or (iii) at least one compound that donates, transfers or releases nitric oxide, induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase and at least one therapeutic agent.

53. The kit of claim 52, wherein the at least one compound that donates, transfers or releases nitric oxide, induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase; the at least one therapeutic agent; or the at least one compound that donates, transfers or releases nitric oxide, induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase and at least one therapeutic agent; are in the form of separate components in the kit

54. A kit comprising the composition of claim 14, 29 or 37.

55. A compound selected from the group consisting of:

1-(1-(cyclohexylmethyl)-3-(hydroxymethyl)pyrazol-5-yl)-4-(methylsulfonyl) benzene;

4-(1-(cyclohexylmethyl)-3-((2-hydroxyethoxy)methyl)pyrazol-5-yl)-1-(methylsulfonyl)benzene;

1-(3-(hydroxymethyl)-1-benzylpyrazol-5-yl)-4-(methylsulfonyl)benzene;
1-(3-((1E)-3-hydroxyprop-1-enyl)-1-(cyclohexylmethyl)pyrazol-5-yl)-4-(methylsulfonyl) benzene;
1-(1-(cyclohexylmethyl)-3-(3-hydroxypropyl)pyrazol-5-yl)-4-(methylsulfonyl)benzene;
1-(1-(cyclohexylmethyl)-3-vinylpyrazol-5-yl)-4-(methylsulfonyl)benzene;
methyl (2E)-3-(1-(cyclohexylmethyl)-5-(4-(methylsulfonyl)phenyl)pyrazol-3-yl) prop-2-enoate;
methyl 5-(4-(methylsulfonyl)phenyl)-1-benzylpyrazole-3-carboxylate;
1-(1-(cyclohexylmethyl)-3-((nitrooxy)methyl)pyrazol-5-yl)-4-(methylsulfonyl)benzene;
4-(1-(cyclohexylmethyl)-3-((2-(nitrooxy)ethoxy)methyl)pyrazol-5-yl)-1-(methylsulfonyl) benzene;
4-(methylsulfonyl)-1-(3-((nitrooxyl)methyl)-1-benzylpyrazol-5-yl)benzene;
1-(3-((1E)-3-nitrooxyprop-1-enyl)-1-(cyclohexylmethyl)pyrazol-5-yl)-4-(methylsulfonyl) benzene;
1-(1-(cyclohexylmethyl)-3-(3-(nitrooxy)propyl)pyrazol-5-yl)-4-(methylsulfonyl) benzene;
3-(4-(methylsulfonyl)phenyl)-5-(trifluoromethyl)(2-pyridyl) phenyl ketone;
2-(3-(4-(methylsulfonyl)phenyl)-5-(trifluoromethyl)(2-pyridyl))-2-phenylethanenitrile;
3-fluorophenyl 2-(4-methylsulfonylphenyl)(3-pyridyl) ketone
2-(4-(methylsulfonyl)phenyl)(3-pyridyl) 2-pyridyl ketone;
ethyl 3-((2-(4-(methylsulfonyl)phenyl)-3-pyridyl)carbonyl)benzoate; or a pharmaceutically acceptable salt thereof.

56. A composition comprising at least one compound of claim 55 and a pharmaceutically acceptable carrier.

57. The composition of claim 56, further comprising (i) at least one compound that donates, transfers or releases nitric oxide, induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase; (ii) at least one therapeutic agent; or (iii) at least one compound that donates, transfers or releases nitric oxide, induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase and at least one therapeutic agent.

58. A kit comprising at least one compound of claim 55.